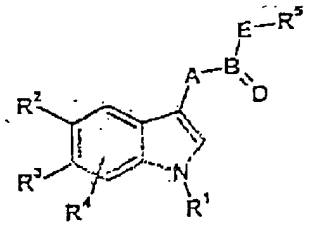
Claims

1. A method for the treatment of a skin disease comprising topically administering a subject in need thereof a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof:



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in which

R^1 is

(i) -C_{1-12}-alkyl, straight-chain or branched-chain or -C_2-C_{12} alkenyl, mono- or polyunsaturated,

optionally mono- or polysubstituted by -OH, -SH, -NH_2, -NHC_{1-6}-alkyl, -$N(C_{1-6}$-alkyl$)_2$, -NHC_{6-14}aryl, -$N(C_{6-14}$aryl$)_2$, -$N(C_{1-6}$alkyl$)(C_{6-14}$aryl), -$NHCOR^6$, -NO_2, -CN, -F, -Cl, -Br, -I, -O-C_{1-6}-alkyl, -O-C_{6-14}-aryl, -$O(CO)R^6$, -S-C_{1-6}-alkyl, -S-C_{6-14}aryl, -SOR^6, -SO_3H, -SO_2R^6, -OSO_2C_{1-6}alkyl, -OSO_2C_{6-14}aryl, -$(CS)R^6$, -COOH, -$(CO)R^6$, mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having 3-14 ring members, mono-, bi- or tricyclic saturated or mono-or polyunsaturated heterocycles having 5-15 ring members and 1-6 heteroatoms, which are preferably N, O and S, wherein the C_{6-14}aryl groups and the carbocyclic and heterocyclic substituents for their part can optionally be mono- or polysubstituted by R^4,

(ii) a mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycle having 3-14 ring members or a mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycle having 5-15 ring members and 1-6 heteroatoms, which are preferably N, O and S, or a carbo- or heterocyclic saturated or mono- or polyunsaturated spirocycle having 3-10 ring members, where heterocyclic systems contain 1-6 heteroatoms, which are preferably N, O and S, optionally mono- or polysubstituted by -OH, -SH, $-NH_2$, $-NHC_{1-6}$-alkyl, $-N(C_{1-6}\text{-alkyl})_2$, $-NHC_{6-14}$aryl, $-N(C_{6-14}\text{aryl})_2$, $-N(C_{1-6}\text{alkyl})(C_{6-14}\text{aryl})$, $-NHCOR^6$, $-NO_2$, -CN, -F, -Cl, -Br, -I, $-O\text{-}C_{1-6}$-alkyl, $-O\text{-}C_{6-14}$-aryl, $-O(CO)R^6$, $-S\text{-}C_{1-6}$-alkyl, $-S\text{-}C_{6-14}$aryl, $-SOR^6$, $-SO_3H$, $-SO_2R^6$, $-OSO_2C_{1-6}$alkyl, $-OSO_2C_{6-14}$aryl, $-(CS)R^6$, -COOH, $-(CO)R^6$, mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having 3-14 ring members, mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having 5-15 ring members and 1-6 heteroatoms, which are preferably N, O and S, wherein the C_{6-14}aryl groups and the carbocyclic and heterocyclic substituents can optionally be mono- or polysubstituted by R^4,

R^5 is

a mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycle having 3-14 ring members or a mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycle having 5-15 ring members and 1-6 heteroatoms, which are preferably N, O and S, or a carbo-or heterocyclic saturated or mono-or polyunsaturated spirocycle having 3-10 ring members, where heterocyclic systems contain 1-6 heteroatoms, which preferably N, O and S, optionally mono- or polysubstituted by -OH, -SH, $-NH_2$, $-NHC_{1-6}$-alkyl, $-N(C_{1-6}\text{-alkyl})_2$, $-NHC_{6-14}$aryl, $-N(C_{6-14}\text{aryl})_2$, $-N(C_{1-6}\text{alkyl})(C_{6-14}\text{aryl})$, $-NHCOR^6$, $-NO_2$, -CN, -F, -Cl, -Br, -I, $-O\text{-}C_{1-6}$-alkyl, $-O\text{-}C_{6-14}$-aryl, $-O(CO)R^6$, $-S\text{-}C_{1-6}$-alkyl, $-S\text{-}C_{6-14}$aryl, $-SOR^6$, $-SO_3H$, $-SO_2R^6$, $-OSO_2C_{1-6}$alkyl, $-OSO_2C_{6-14}$aryl, $-(CS)R^6$, -COOH, $-(CO)R^6$, mono-, bi-

or tricyclic saturated or mono- or polyunsaturated carbocycles having 3-14 ring members, mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having 5-15 ring members and 1-6 heteroatoms, which are preferably N, O and S, wherein the C_{6-14}aryl groups and the carbocyclic and heterocyclic substituents can optionally be mono- or polysubstituted by R^4, with the proviso that R^5 contains at least one substituent selected from -F, -Cl, -Br, -I;

R^2, R^3 are hydrogen or -OH, where at least one of the two substituents must be -OH;

R^4 is

-H, -OH, -SH, $-NH_2$, $-NHC_{1-6}$-alkyl, $-N(C_{1-6}\text{-alkyl})_2$, $-NHC_{6-14}$aryl, $-N(C_{6-14}\text{aryl})_2$, $-N(C_{1-6}\text{alkyl})(C_{6-14}\text{aryl})$, $-NHCOR^6$, $-NO_2$, -CN, -COOH, $-(CO)R^6$, $-(CS)R^6$, -F, --Cl, -Br, -I, $-O-C_{1-6}$-alkyl, $-O-C_{6-14}$-aryl, $-O(CO)R^6$, $-S-C_{1-6}$-alkyl, $-S-C_{6-14}$aryl, $-SOR^6$, $-SO_2R^5$, $-C_1-C_6$-alkyl, wherein each aryl or alkyl may be mono- or polysubstituted by -OH, -F, -Cl, -Br, -I;

R^6 is

-H, $-NH_2$, $-NHC_{1-6}$-alkyl, $-N(C_{1-6}\text{-alkyl})_2$, $-NHC_{6-14}$aryl, $-N(C_{6-14}\text{aryl})_2$, $-N(C_{1-6}\text{alkyl})(C_{6-14}\text{aryl})$, $-O-C_{1-6}$-alkyl, $-O-C_{6-14}$-aryl, $-S-C_{1-6}$-alkyl, $-S-C_{6-14}$aryl,

$-C_{1-12}$-alkyl, straight-chain or branched-chain,

$-C_{2-12}$-alkenyl, mono- or polyunsaturated, straight-chain or branched-chain,

mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having 3-14 ring members,

mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having 5-15 ring members and 1-6 heteroatoms, which are preferably N, O and S;

A is either a bond, or

$-(CH_2)_m-$, $-(CH_2)_m-(CH=CH)_n-(CH_2)_p-$, $-(CHOZ)_m-$, -(C=O)-, -(C=S)-, -(C=N-Z)-, -O-, -S-, -NZ-,

wherein m, p = 0-3 and n = 0-2 and
Z is
-H, or
-C_{1-12}-alkyl, straight-chain or branched-chain,
-C_{2-12}-alkenyl, mono- or polyunsaturated, straight-chain or branched-chain,
mono-, bi- or tricyclic saturated or mono- or polyunsaturated carbocycles having 3-14 ring members,
mono-, bi- or tricyclic saturated or mono- or polyunsaturated heterocycles having 5-15 ring members and 1-6 heteroatoms, which are preferably N, O and S;
B is either carbon or sulfur, or -(S=O)-;
D is oxygen sulfur, CH_2 or N-Z,
where, if B is carbon, D is S or CH_2;
E is a bond, or
-$(CH_2)_m$-, -O-, -S-, -(N-Z)-, wherein m and Z have the meaning already described above.

2. The method of claim 1 wherein R^5 is selected from monocyclic saturated or mono- or polyunsaturated carbocycles and heterocycles having at least one halogen substituent.

3. The method of claim 2 wherein R^5 is is selected from monocyclic aromatic carbocycles and heterocycles having at least one halogen substituent.

4. The method of claim 3 wherein R^5 is a pyridine ring having at least one halogen substituent.

5. The method of claim 3 wherein R^5 is a phenyl ring having at least one halogen substituent.

6. The method of claim 1 wherein R^1 is selected from C_1-C_{12} alkyl, which is optionally substituted.

7. The method of claim 1 wherein R^1 is selected from monocyclic saturated or mono-or polyunsaturated carbocycles or heterocycles, which are optionally substituted.

8. The method of claim 1 wherein R^2 is OH and R^3 is H.

9. The method of claim 1 wherein A is selected from -(C=O)- and -(CHOH)-.

10. The method of claim 1 wherein B is C.

11. The method of claim 1 wherein D is O.

12. The method of claim 1 wherein E is -(N-H)-.

13. The method of claim 1 wherein compound (I) is (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide).

14. The method of any one of claims 1-13 wherein the skin disease is an allergic and/or inflammatory disease.

15. The method of claim 14 wherein the allergic disease is allergic dermatitis.

16. The method of any one of claims 1-15 wherein the compound is administered to a skin area which is afflicted by disease.

17. The method of claim 16 wherein the compound is administered after an allergic challenge.

18. The method of claim 17 wherein the compound is administered up to 48 h after the allergic challenge.

19. The method of any one of claims 1-18 wherein the compound (I) is co-administered with at least one further pharmaceutical agent.

20. The method of claim 19 wherein the further pharmaceutical agent is a drug stimulating cAMP production.

21. The method of claim 20 wherein the further pharmaceutical agent is a corticosteroid.